CHAPTER 23

FUTURE DIRECTIONS

The scope and complexity of the AFHS has required gradual refinement and correction to meet the challenges of changing technology and scientific direction, and to ensure continued participation of all enrolled members. This chapter outlines some of the changes incorporated in the fifth-year followup examination and identifies several areas of future work expected to significantly augment the study.

FIFTH-YEAR FOLLOWUP EXAMINATION

Since the fifth-year followup examination was initiated prior to the full analysis of the data from the third-year examination, most modifications were founded upon quality control issues and the desire to make the clinical content of the examination more responsive to the medical needs of the participants.

Clinical quality control enhancements were made to improve measurement techniques. The digit preference noted in systolic and diastolic blood pressure readings led to the use of automated blood pressure recording; all other parameters of the blood pressure readings (e.g., sitting position, three recordings, nondominant arm at heart level) were not changed.

The problem in skin test reading was met by a rigorous quality control plan that included the following elements: refresher training for readers; a required reading of the four skin tests of all participants by both readers, each blind to the results of the other; a required reread of 10 percent of all tests by each of the readers, each blind to the previous reading; and a required weekly report citing numbers and proportions of participants with possible anergy, reversal of induration-erythema measurements, and untoward skin reactions or other reading problems (e.g., participant refusal).

In addition, new skin test forms were developed to facilitate accurate recording and transcription; specific clinical criteria were formulated to require consultation by an allergist; and the skin test measurement criterion for possible anergy, consistent with current World Health Organization guidelines, was adopted for the clinical interpretation of all skin test readings. It is anticipated that this clinical quality control program will standardize both readings and interpretations, and will produce a uniformly superior data set.

EXPOSURE INDEX REFINEMENTS

Since the development of the Study Protocol and the analysis of the 1982 Baseline data, there has been concern among some scientists and the principal

investigators over the accuracy and validity of the exposure estimates. It is unclear whether statistically significant differences in some variables between the Ranch Hand and Comparison groups, unsupported by dose-response estimates, have been due to chance, or whether true differences are obscured by an inadequate exposure index or group misclassification.

In mid-1986, strong correlations between dioxin levels in fat tissue and serum were demonstrated by the CDC and other institutions. Because of these results, the Air Force is currently engaged in a collaborative study with CDC to determine whether serum dioxin levels vary significantly in the Ranch Hand population. Approximately 200 AFHS volunteers have supplied a pint of blood to be analyzed for dioxin at the CDC laboratories. If clear and meaningful exposure findings are evident from this study, several additional studies are feasible: testing can be expanded to the entire study population and a meaningful exposure index based on total current TCDD body burden may be developed; and by means of archived AFHS serum samples from the Baseline study, it may be possible to calculate a reasonably precise half-life of TCDD in humans. These expanded studies will allow the estimation of body burdens of TCDD at the time of departure from SEA (assuming the absence of intervening vocational and recreational exposures).

If, in fact, these potential studies become reality within the next 2 years, the fifth-year followup study data will be statistically analyzed using a more appropriate exposure index. In anticipation of this advance, the AFHS is currently collecting 280 to 350 ml of blood from all volunteers attending the fifth-year followup study.

ADDITIONAL ANALYSES AND STUDIES

As in the 1984 Baseline Report, not all of the measured dependent variables were subjected to statistical analysis (e.g., prothrombin, leutinizing hormone, follicle stimulating hormone), largely because they were not within the bounds of the Air Force-prescribed analyses. Exploration of many of the unanalyzed variables is contemplated as time and resources permit. Similarly, many analytic opportunities to define possible symptom-clinical sign clusters or syndromes by multivariate analysis of variance techniques were passed over due to time and charter. Particularly challenging as an area of future work may be the changing relationships of some immunological variables over time and the biological impact of these changes on the induction of diseases such as cancer. Likewise, future efforts to define shifting cardiovascular disease patterns are a logical extension of the rich longitudinal data base of the AFHS. Such efforts await future analysis and publication.

The assessment of possible selection and participation bias has been addressed in a comprehensive manner in this report (see Chapter 5). The analyses and discussion suggest that statistical use of the total Comparison group (versus the Original Comparison group) is justified in this report, and that the impact of selection and participation biases have been minimal. As the followup studies continue, it is anticipated that a wealth of data on

compliance-participation factors will be available for continued comprehensive bias analyses. In particular, it is hoped that more complete data will exist to examine the true differences in current health status between refusals and their replacements. As the data set grows over time, the bias analyses will become more complex and will have to deal with changing motivations of the participants to continue in this study. Such bias analyses and assessments will always be of great importance to this study as they ultimately set the bounds for an inference on herbicide causality.